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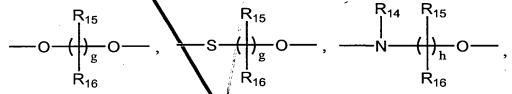
Abstract

This invention is directed to the use of diaryl acid derivatives of formula (I) and their pharmaceutical compositions as PPAR ligand receptor binders. The PPAR ligand receptor binders of this invention are useful as agonists or antagonists of the PPAR receptor

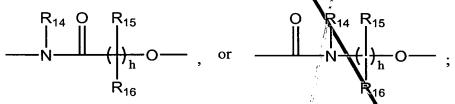
wherein: R_1 R_2 R_3 R_4 R_5 R_6 R_8 R_8

and are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;

A is -O-, -S-, -SO-, -SO₂-, -NR₁₃-, -C(O), -N(R₁₄)C(O)-, -C(O)N(R₁₅)-, -N(R₁₄)C(O)N(R₁₅)-, -C(R₁₄)=N-,



a chemical bond,



B is -O-, -S-, $-NR_{19}$ -, a chemical bond, -C(O)-, $-N(R_{20})C(O)$ -, or $-C(O)N(R_{20})$ -;

- 15 E is a chemical bond or an ethylene group;
 - a is 0-6;
 - b is 0-4;
 - c is 0-4;
 - d is 0-6;
- 20 g is 1-5;
 - h is 1-4;

 R_1 , R_3 , R_5 and R_7 , are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl; R_2 , R_4 , R_6 and R_8 , are independently -(CH₂)_q-X; q is 0-3;

X hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO2-, - SR_{23} , Y^1Y^2N - or Y^3Y^4NCO -:

 Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is

hydrogen or alkyl and the other of Y¹ and Y² is acyl or arovl: 5 Y³ and Y⁴ are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl; Z is R₂₁O₂C-, R₂₁OC-, cýclo-imide, -CN, R₂₁O₂SHNCO-, R₂₁O₂SHN-, (R₂₁)₂NCO-, R₂₁O- 2,4thiazolidinedionyl, or tetrazolyl; and

R₁₉ and R₂₁ are independently hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

10 R₁₃, R₁₇, R₁₉ and R₂₃ are independently R₂₂OC-, R₂₂NHOC-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl

R₁₄, R₁₅, R₁₆, R₁₈ and R₂₀ are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl: or R₁₄, and R₁₅ taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-6, then at least one pair of vicinal R₁ radicals taken together with the carbon atoms to which 15

the R₁ radicals are linked form a

when b is 2-4, then at least one pair of vicinal R3 radicals taken together with the carbon atoms to which

the R₃ radicals are linked form a

when c is 2-4, then at least one pair of vicinal R5 radicals taken together with the carbon atoms to which

20 the R₅ radicals are linked form a

group; or

when d is 2-6, then at least one pair of vicinal R₇ radicals taken together with the carbon atoms to which

the R₇ radicals are linked form a

R₈ group, or a 5-membered cycloalkyl group, or

when d is 2-6, then at least one pair of non-vicinal R7 radicals taken together with the carbon atoms to which the R₇ radicals are linked form a 5-membered cycloalkyl group; or

25 geminal R5 and R6 radicals taken together with the carbon atom through which these radicals are linked form a 5 membered cycloalkyl group; or

geminal R7 and R8 radicals taken together with the carbon atom through which these radicals are linked form a 5 membered cycloalkyl group; and

R₂₂ is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

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